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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,744	12/21/2001	Richard Soltoro	9233-71	3700
20792	7590	07/08/2004	EXAMINER	
MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627			TELLER, ROY R	
			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 07/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/036,744	SOLTERO ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Roy Teller	1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 07 April 2004.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-53,248-281,371-398 and 446-458 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-53, 248-281, 371-398, and 446-458 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____.

## DETAILED ACTION

This office action is in response to the action, received 4/7/04.

Claims 1-53, 248-281, 371-398, and 446-458 are pending.

### *Claim Rejections - 35 USC § 102*

Claims 1-53, 248-281, 371-398, and 446-458 stand rejected under 35 USC 102 (B) as being anticipated by Ekwuribe (USPN 6,309,633) for the reasons set forth in the previous office action which are restated below.

Ekwuribe teaches a drug-oligomer conjugate, wherein D is a therapeutic drug moiety, H and H' are each a hydrophilic moiety, and L is a lipophilic moiety. The therapeutic drug moiety is preferably insulin or a functional equivalent thereof, see abstract, claim 1 and claim 4. Ekwuribe teaches various oligomers, see column 10, lines 1-3. Ekwuribe discloses synthesis of chemically modified insulin with oligomers has been accomplished, see column 29, lines 1-3.

Applicant's arguments were carefully considered but were not found persuasive.

Applicant contends that Ekwuribe does not teach coupling an oligomer with a proinsulin polypeptide which results in coupling of the oligomer to the insulin polypeptide portion thereof. Further, Ekwuribe does not describe that one or more peptides are cleaved from the conjugate to provide the insulin polypeptide-oligomer conjugate. However, the Ekwuribe reference teaches a drug-oligomer conjugate which reads upon insulin (see, e.g., for example, column 4).

Furthermore, the Ekwuribe reference discloses that the length and composition of the lipophilic components and the hydrophilic components may be adjusted where the conjugate is to be administered (see, e.g., for example, column 5).

Therefore, the reference is deemed to anticipate the instant claims above, especially in the absence of clear and convincing evidence to the contrary.

***Claim Rejections - 35 USC § 103***

Claims 1-53, 248-281, 371-398, and 446-458 stand rejected under 35 USC 103 (a) as being unpatentable over Ekwuribe (USPN 6,309,633) for the reasons set forth in the previous office action which are restated below.

Based upon the beneficial overall teachings provided by Ekwuribe with respect to synthesis of chemically modified insulin with oligomers, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Applicant's arguments were carefully considered but were not found persuasive.

Applicant contends that Ekwuribe does not teach or suggest the novel and unexpected conjugate then cleave approach as claimed. However, the Ekwuribe reference teaches a drug-oligomer conjugate and discloses that the length and composition of the lipophilic components and the hydrophilic components may be adjusted where the conjugate is to be administered.

Thus, the invention as a whole is *prima facie* obvious over the reference, especially in the absence of clear and convincing evidence to the contrary.

***Conclusion***

All claims are rejected.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This application contains claims 54-247, 282-370, 399-445, and 459-467, drawn to an invention nonelected with traverse in Paper 0903. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy Teller whose telephone number is 571-272-0971. The examiner can normally be reached on Monday-Friday from 5:30 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RT  
1654  
7/7/04



CHRISTOPHER R. TATE  
PRIMARY EXAMINER